

Practitioner's Docket No. MPI02-110P1RNM

U.S.S.N. 10/678,872

RESPONSE

Originally, claims 1-24 were pending in the above-referenced application. After entry of the amendment detailed above, claims 1-24 have been canceled, and claims 25-44 are now pending. The subject matter of original claims 1-7 and 20-24, now canceled, will be pursued in a continuation application. Applicants would also like to point out that original claims 8-19 have been re-presented as claims 25-27, 32-39, and 44 to avoid any confusion in the amendment of the claims. Specifically, certain of the original claims 8-19 (now claims 25-27, 32-39, and 44) include compound names and substituents that incorporate brackets as part of the name and/or substituent and thus any amendments to the claims that include deletion of subject matter (and showing this by using brackets) would lead to confusion in determining which subject matter is to be deleted.

Claim Amendments and Additions:

Applicants have re-presented original claims 10, 11, 12, 13, 14, and 16 as claims 27, 32, 33, 34, and 35, respectively, with some amendments. Amendments to these claims were made to delete redundant material. For example, each of the original claims made specific reference to a previous claim to define a particular substituent (e.g., original claim 13 states "where R¹¹ is defined in Claim 8". Applicants respectfully submit that this specific reference is not necessary since the claims necessarily incorporate the limitations of the claims upon which they are dependent. Accordingly, new claims 27, 32, 33, 34, and 35 do not include the specific claim reference to define a substituent.

Applicants have also added new claims 28-31, and 40-43. Applicants respectfully submit that no new matter is presented with these claims and support for these new claims can be found throughout the specification and in the claims as originally filed.

Rejection under 35 U.S.C. 112, first and second paragraphs:

The Examiner has rejected claims 1-7 and 20-24 under 35 U.S.C. §112, first and second paragraphs. As detailed above, claims 1-7 and 20-24 have been canceled in this application and the subject matter will be pursued in a continuation application. Accordingly, the rejections are now moot.

Rejection under 35 U.S.C. § 102

The Examiner has rejected claims 1-5, 8-13, 17 and 19 under 35 U.S.C. § 102(b). Applicants would again like to point out that claims 1-5 have been canceled with this amendment and will be pursued in a continuation application. Additionally, claims 1-5 pertain to methods of inhibiting CRTh2 and the abstracts the Examiner has cited below do not teach the use of these compounds as inhibitors of CRTh2. Accordingly, Applicants address the Examiner's rejections with respect to original claims 8-13, 17 and 19 below (now claims 25-27, 32-34, 38, and 44).

(Page 16 of 21)

Practitioner's Docket No. **MPI02-110P1RNM**

U.S.S.N. 10/678,872

The Examiner has stated that the subject matter of the rejected claims are anticipated by Zalukajevs (CA 48:56687 and CA 62:22149) and Funabashi (72:31075). The Examiner has further stated that Zalukajevs and Funabashi both teach 4-anilino-1-benzoyl-1,2,3,4-tetrahydroquinolidine.

Applicants respectfully submit that the subject matter of original claims 8-13, 17 and 19 (now claims 25-27, 32-34, 38, and 44) are not anticipated by Zalukajevs or Funabashi. Specifically, claim 8 recites the following: "provided that when X_2 is a bond, SO or SO_2 , then R^4 is not H" and thus 4-anilino-1-benzoyl-1,2,3,4-tetrahydroquinolidine is excluded from the scope of claim 8 (and claims dependent thereon).

The Examiner has also rejected original claims 1-5, 8-13, 17 and 19 (now claims 25-27, 32-34, 38, and 44) as being anticipated by Zalukajevs (CA 59:54789, 67:53250 and CA 65:15179e-g) and has further stated that Zalukajevs teaches N-(1-benzoyl-1,2,3,4-tetrahydro-2-methyl-4-quinoliny)-N-phenylacetamide or a N-(1-benzoyl-6(Cl or Br)-1,2,3,4-tetrahydro-2-methyl-4-quinoliny)-N-phenyl acetamide.

Applicants respectfully submit that original claims 8-13, 17 and 19 (now claims 25-27, 32-34, 38, and 44) are not anticipated by Zalukajevs (CA 59:54789, 67:53250 and CA 65:15179e-g) because N-(1-benzoyl-1,2,3,4-tetrahydro-2-methyl-4-quinoliny)-N-phenylacetamide, N-(1-benzoyl-6-Cl-1,2,3,4-tetrahydro-2-methyl-4-quinoliny)-N-phenyl acetamide, and N-(1-benzoyl-6-Br-1,2,3,4-tetrahydro-2-methyl-4-quinoliny)-N-phenyl acetamide are included in the proviso at the end of original claim 8 (now claim 25), and thus are excluded from the scope of original claim 8 (and claims dependent thereon).

For the Examiner's convenience, Applicants have reproduced the proviso in original claim 8 (now claim 25) directly below and have underlined the above-referenced compounds to highlight where they are located in the proviso.

"provided that the compound is not 2-methyl-N-phenyl-N-[1,2,3,4-tetrahydro-2-methyl-1-(2-methyl-1-oxobutyl)-4-quinoliny]-butamide; N-(1-Acetyl-1,2,3,4-tetrahydro-2-methyl-4-quinoliny)-N-phenyl-heptamide; N-phenyl-N-[1,2,3,4-tetrahydro-2-methyl-1-(1-oxo-3-phenylpropyl)-4-quinoliny]- benzenepropanamide; N-phenyl-N-[1,2,3,4-tetrahydro-2-methyl-1-(3-nitrobenzoyl)-4-quinoliny]- hexanamide; N-[1,1'-biphenyl]-3-yl-N-[1,2,3,4-tetrahydro-1-(4-methoxybenzoyl)-2-methyl-4-quinoliny]-acetamide; N-(1-benzoyl-1,2,3,4-tetrahydro-2-methyl-4-quinoliny)-N-(4-nitrophenyl)- heptanamide; N-(1-benzoyl-1,2,3,4-tetrahydro-2-methyl-4-quinoliny)-N-(4-methoxyphenyl)-2-methyl- propanamide; N-[1-(4-fluorobenzoyl)-1,2,3,4-tetrahydro-2-methyl-4-quinoliny]-N-phenyl- butanamide; N-phenyl-N-[1,2,3,4-tetrahydro-1-(3-methoxybenzoyl)-2-methyl-4-quinoliny]-pentanamide; 2-ethyl-N-[1-(2-ethyl-1-oxobutyl)-1,2,3,4-tetrahydro-2,8-dimethyl-4-quinoliny]-N-(2-methylphenyl)-butanamide; N-[1-[(4-fluorophenyl)acetyl]-1,2,3,4-tetrahydro-2-methyl-4-quinoliny]-N-phenyl- propanamide; N-phenyl-N-[1,2,3,4-tetrahydro-2-methyl-1-(4-nitrobenzoyl)-4-quinoliny]-octanamide; N-cyclohexyl-4-[(cyclohexylamino)carbonyl]phenylamino]-3,4-dihydro-2-methyl-1(2H)-quinolinecarboxamide; N-

(Page 17 of 21)

Practitioner's Docket No. MPI02-110P1RNM

U.S.S.N. 10/678,872

[1-(4-ethylbenzoyl)-1,2,3,4-tetrahydro-2,8-dimethyl-4-quinolinyl]-N-(2-methylphenyl)-3-(4-nitrophenyl)-2-propenamide; 3-(4-methoxyphenyl)-N-phenyl-N-[1,2,3,4-tetrahydro-1-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-quinolinyl]-2-propenamide; 4-[(ethoxyoxoacetyl)phenylamino]-3,4-dihydro-2-methyl- γ -oxo-ethyl ester-1(2H)-quinolineacetic acid; N-[1-(3-cyclohexyl-1-oxopropyl)-1,2,3,4-tetrahydro-2-methyl-4-quinolinyl]-N-phenyl-cyclohexanepropanamide; 4-(acetylphenylamino)-3,4-dihydro-2-methyl-gamma-oxo-1(2H)-quinolinepentanoic acid; N-(1-benzoyl-1,2,3,4-tetrahydro-2-methyl-4-quinolinyl)-2,2-dimethyl-N-phenyl-propanamide; N-(1-benzoyl-6-bromo-1,2,3,4-tetrahydro-2-methyl-4-quinolinyl)-N-phenyl-pentanamide; N-[1-(2-furanylcarbonyl)-1,2,3,4-tetrahydro-2-methyl-4-quinolinyl]-N-phenyl-acetamide; 2-methyl-N-phenyl-N-[1,2,3,4-tetrahydro-1-(3-methoxybenzoyl)-2-methyl-4-quinolinyl]-propanamide; N-[1-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)acetyl]-1,2,3,4-tetrahydro-2-methyl-4-quinolinyl]-N-phenyl-acetamide; 2,2,2-trifluoro-N-phenyl-N-[1,2,3,4-tetrahydro-1-(3-methoxybenzoyl)-2-methyl-4-quinolinyl]-acetamide; 2-ethyl-N-[1-(2-ethyl-1-oxobutyl)-1,2,3,4-tetrahydro-2-methyl-4-quinolinyl]-N-phenyl-butanamide; N-(1-benzoyl-1,2,3,4-tetrahydro-2-methyl-4-quinolinyl)-N-(3-methoxyphenyl)-acetamide; N-phenyl-N-[1,2,3,4-tetrahydro-2-methyl-1-(1-oxohexyl)-4-quinolinyl]-acetamide; N-(1-acetyl-1,2,3,4-tetrahydro-2-methyl-4-quinolinyl)-N-phenyl-2-thiophenecarboxamide; N-[1-(2-fluorobenzoyl)-1,2,3,4-tetrahydro-2-methyl-4-quinolinyl]-N-phenyl-hexanamide; N-phenyl-N-[1,2,3,4-tetrahydro-1-(4-methoxybenzoyl)-2-methyl-4-quinolinyl]-hexanamide; N-phenyl-N-[1,2,3,4-tetrahydro-1-(4-methoxybenzoyl)-2-methyl-4-quinolinyl]-hexanamide; N-[1-(cyclopropylcarbonyl)-1,2,3,4-tetrahydro-2-methyl-4-quinolinyl]-N-phenyl-cyclopropanecarboxamide; N-(1-benzoyl-1,2,3,4-tetrahydro-2-methyl-4-quinolinyl)-N-(4-methylphenyl)-acetamide; 2-methyl-N-phenyl-N-[1,2,3,4-tetrahydro-2-methyl-1-(2-methyl-1-oxopropyl)-4-quinolinyl]-propanamide; N-phenyl-N-[1,2,3,4-tetrahydro-1-(4-methoxybenzoyl)-2-methyl-4-quinolinyl]-2-thiophenecarboxamide; 1-(3,5-dinitrobenzoyl)-N-formyl-1,2,3,4-tetrahydro-2-methyl-N-phenyl-4-quinolinamine; N-[1-(4-chloro-3-nitrobenzoyl)-1,2,3,4-tetrahydro-2-methyl-4-quinolinyl]-N-phenyl-acetamide; N-phenyl-N-[1,2,3,4-tetrahydro-2-methyl-1-(3-nitrobenzoyl)-4-quinolinyl]-acetamide; N-phenyl-N-[1,2,3,4-tetrahydro-1-(3-methoxybenzoyl)-2-methyl-4-quinolinyl]-hexanamide; N-[1-(2-furanylcarbonyl)-1,2,3,4-tetrahydro-2-methyl-4-quinolinyl]-N-phenyl-2-furancarboxamide; N-phenyl-N-[1,2,3,4-tetrahydro-2-methyl-1-(1-oxopropyl)-4-quinolinyl]-acetamide; N-phenyl-N-[1,2,3,4-tetrahydro-1-[3-(4-methoxyphenyl)-1-oxo-2-propenyl]-2-methyl-4-quinolinyl]-acetamide; 3-(2-furanyl)-N-[1-[3-(2-furanyl)-1-oxo-2-propenyl]-1,2,3,4-tetrahydro-2-methyl-4-quinolinyl]-N-phenyl-2-propenamide; N-[1-[2-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-1-oxo-3-phenylpropyl]-1,2,3,4-tetrahydro-2-methyl-4-quinolinyl]-N-phenyl-octanamide; N-[1-(3-chlorobenzoyl)-1,2,3,4-tetrahydro-2-methyl-4-quinolinyl]-N-phenyl-acetamide; Relative stereochemistry N-phenyl-N-

(Page 18 of 21)

Practitioner's Docket No. MPI02-110P1RNM

U.S.S.N. 10/678,872

[(2R,4S)-1,2,3,4-tetrahydro-2-methyl-1-(1-oxopropyl)-4-quinoliny]-acetamide; Relative stereochemistry N-[(2R,4S)-1-benzoyl-1,2,3,4-tetrahydro-2-methyl-4-quinoliny]-2-methyl-N-phenyl-propanamide; Relative stereochemistry N-[(2R,4S)-1-acetyl-1,2,3,4-tetrahydro-2-methyl-4-quinoliny]-N-phenyl-hexanamide; Relative stereochemistry N-[(2R,4S)-1-acetyl-1,2,3,4-tetrahydro-2-methyl-4-quinoliny]-N-phenyl-propanamide; Relative stereochemistry N-[(2R,4S)-1-acetyl-1,2,3,4-tetrahydro-2-methyl-4-quinoliny]-N-phenyl-heptanamide; Relative stereochemistry N-[(2R,4S)-1-benzoyl-1,2,3,4-tetrahydro-2-methyl-4-quinoliny]-2,2-dimethyl-N-phenyl-propanamide; N-[1-(3-fluorobenzoyl)-1,2,3,4-tetrahydro-2-methyl-4-quinoliny]-N-phenyl-acetamide; N-[1-[4-(1,1-dimethylethyl)benzoyl]-1,2,3,4-tetrahydro-2-methyl-4-quinoliny]-N-phenyl-acetamide; N-(1-acetyl-1,2,3,4-tetrahydro-2-methyl-4-quinoliny)-2-methyl-N-phenyl-propanamide; 2,2,2-trifluoro-N-phenyl-N-[1,2,3,4-tetrahydro-2-methyl-1-(trifluoroacetyl)-4-quinoliny]-acetamide; Relative stereochemistry N-[(2R,4S)-1-acetyl-1,2,3,4-tetrahydro-2-methyl-4-quinoliny]-2,2-dimethyl-N-phenyl-propanamide; Relative stereochemistry N-[(2R,4S)-1-acetyl-1,2,3,4-tetrahydro-2-methyl-4-quinoliny]-N-phenyl-butanamide; Relative stereochemistry N-[(2R,4S)-1-benzoyl-1,2,3,4-tetrahydro-2-methyl-4-quinoliny]-N-phenyl-acetamide; Relative stereochemistry N-phenyl-N-[(2R,4S)-1,2,3,4-tetrahydro-2-methyl-1-(1-oxoheptyl)-4-quinoliny]-acetamide; Relative stereochemistry N-phenyl-N-[(2R,4S)-1,2,3,4-tetrahydro-2-methyl-1-(1-oxohexyl)-4-quinoliny]-acetamide; Relative stereochemistry N-[(2R,4S)-1-acetyl-1,2,3,4-tetrahydro-2-methyl-4-quinoliny]-N-phenyl-pentanamide; N-phenyl-N-[1,2,3,4-tetrahydro-2-methyl-1-(1-oxo-3-phenyl-2-propenyl)-4-quinoliny]-acetamide; Relative stereochemistry N-[(2R,4S)-1-benzoyl-1,2,3,4-tetrahydro-2-methyl-4-quinoliny]-N-phenyl-heptanamide; Relative stereochemistry N-[(2R,4S)-1-acetyl-1,2,3,4-tetrahydro-2-methyl-4-quinoliny]-N-phenyl-acetamide; Relative stereochemistry N-[(2R,4S)-1-benzoyl-1,2,3,4-tetrahydro-2-methyl-4-quinoliny]-N-phenyl-pentanamide; N-phenyl-N-[1,2,3,4-tetrahydro-2-methyl-1-(tricyclo[3.3.1.1^{3,7}]dec-1-ylcarbonyl)-4-quinoliny]-acetamide; N-phenyl-N-[1,2,3,4-tetrahydro-2-methyl-1-(1-oxopropyl)-4-quinoliny]-propanamide; N-phenyl-N-[1,2,3,4-tetrahydro-2-methyl-1-(2-thienylcarbonyl)-4-quinoliny]-acetamide; N-phenyl-N-[1,2,3,4-tetrahydro-1-(4-methoxybenzoyl)-2-methyl-4-quinoliny]-2-furancarboxamide; N-phenyl-N-[1,2,3,4-tetrahydro-1-(4-methoxybenzoyl)-2-methyl-4-quinoliny]-acetamide; N-[1-(3,5-dinitrobenzoyl)-1,2,3,4-tetrahydro-2-methyl-4-quinoliny]-N-phenyl-acetamide; N-phenyl-N-[1,2,3,4-tetrahydro-2-methyl-1-(4-nitrobenzoyl)-4-quinoliny]-acetamide; N-phenyl-N-[1,2,3,4-tetrahydro-1-(2-iodobenzoyl)-2-methyl-4-quinoliny]-acetamide; N-phenyl-N-[1,2,3,4-tetrahydro-2-methyl-1-(2-methyl-1-oxopropyl)-4-quinoliny]-acetamide; N-phenyl-N-[1,2,3,4-tetrahydro-2-methyl-1-[(4-methylphenyl)sulfonyl]-4-quinoliny]-acetamide; N-phenyl-N-[1,2,3,4-tetrahydro-2-methyl-1-[(4-nitrophenyl)methyl]-4-quinoliny]-acetamide; N-phenyl-N-[1,2,3,4-tetrahydro-1-(3-

(Page 19 of 21)

Practitioner's Docket No. MPI02-110P1RNM

U.S.S.N. 10/678,872

methoxybenzoyl)-2-methyl-4-quinolinyl]- acetamide; N-(1-acetyl-1,2,3,4-tetrahydro-2-methyl-4-quinolinyl)-N-phenyl- butanamide; N-phenyl-N-[1,2,3,4-tetrahydro-2-methyl-1-(1-oxobutyl)-4-quinolinyl]- acetamide; N-(1-benzoyl-1,2,3,4-tetrahydro-2-methyl-4-quinolinyl)-N-phenyl-hexanamide; N-(1-benzoyl-1,2,3,4-tetrahydro-2-methyl-4-quinolinyl)-N-phenyl-pentanamide; N-(1-benzoyl-1,2,3,4-tetrahydro-2-methyl-4-quinolinyl)-N-phenyl-propanamide; 1-benzoyl-1,2,3,4-tetrahydro-4-(N-phenylacetamido)quinaldine; N-(1-acetyl-6-bromo-1,2,3,4-tetrahydro-2-methyl-4-quinolinyl)-N-phenyl-acetamide; N-(1-acetyl-1,2,3,4-tetrahydro-2-methyl-6-nitro-4-quinolyl)-acetanilide; N-(1-acetyl-6-chloro-1,2,3,4-tetrahydro-2-methyl-4-quinolyl)-acetanilide; N-(1-acetyl-1,2,3,4-tetrahydro-2-methyl-4-quinolinyl)-N-phenyl-acetamide; N-(1-benzoyl-6-bromo-1,2,3,4-tetrahydro-2-methyl-4-quinolinyl)-N-phenyl-acetamide; N-(1-benzoyl-6-chloro-1,2,3,4-tetrahydro-2-methyl-4-quinolinyl)-N-phenyl-acetamide; N-(1-benzoyl-1,2,3,4-tetrahydro-2-methyl-4-quinolinyl)-N-phenyl- butanamide; N-phenyl-N-[1,2,3,4-tetrahydro-1-(3-fluorobenzoyl)-2-methyl-4-quinolinyl]-hexanamide ; N-[1-(3-chloro-benzoyl)-2-methyl-1,2,3,4-tetrahydro-quinolin-4-yl]-N-phenyl-acetamide; N-[1-(4-fluoro-benzoyl)-2-methyl-6-nitro-1,2,3,4-tetrahydro-quinolin-4-yl]-N-phenyl-acetamide; pentanoic acid (1-benzoyl-6-bromo-2-methyl-1,2,3,4-tetrahydro-quinolin-4-yl)-phenyl-amide; N-(1-benzoyl-6-chloro-2-methyl-1,2,3,4-tetrahydro-quinolin-4-yl)-N-phenyl-acetamide; N-[6-chloro-1-(4-fluoro-benzoyl)-2-methyl-1,2,3,4-tetrahydro-quinolin-4-yl]-N-phenyl-acetamide; N-[6-bromo-1-(4-fluoro-benzoyl)-2-methyl-1,2,3,4-tetrahydro-quinolin-4-yl]-N-phenyl-acetamide; N-(1-benzoyl-6-nitro-2-methyl-1,2,3,4-tetrahydro-quinolin-4-yl)-N-phenyl-acetamide; N-(1-benzoyl-2-methyl-1,2,3,4-tetrahydro-quinolin-4-yl)-N-phenyl-butyramide; N-[1-(3-methoxybenzoyl)-2-methyl-1,2,3,4-tetrahydro-quinolin-4-yl]-2,2-dimethyl-N-phenyl-propionamide.”

In view of the remarks detailed above, Applicants respectfully request that the rejection under 35 U.S.C. § 102(b) be withdrawn by the Examiner.

Claim Objections

The Examiner has objected to original claims 14-16 and 18 (now claims 35-37, and 39) as being dependent from a rejected base claims. For the reasons discussed above, Applicants respectfully submit that original claims 8-13, 17 and 19 (now claims 35-37, and 39) are in condition for allowance and thus Applicants respectfully request that the objection to original claims 14-16 and 18 (now claims 35-37, and 39) be withdrawn.

REMARKS

Entry of the amendments and arguments made herein is respectfully requested, and Applicants respectfully submit that pending claims 25-44 are in condition for allowance. Applicants would additionally like to thank the Examiner for careful review of the application. If the Examiner believes

(Page 20 of 21)

Practitioner's Docket No. MPI02-110P1RNM

U.S.S.N. 10/678,872

that a telephone call would expedite prosecution of the above-referenced application, the Examiner is invited to call the undersigned at (617) 444-3227.

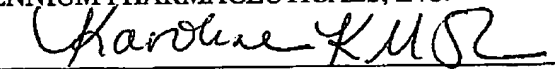
Applicants respectfully request an extension of time from September 29, 2005 up to and including December 29, 2005. In the event any additional fees are necessary, the undersigned hereby authorizes the requisite fees to be charged to Deposit Account No. 501668.

December 28, 2005

Respectfully submitted,

MILLENNIUM PHARMACEUTICALS, INC.

By



Karoline K. M. Shair
Registration No. 44,332
40 Landsdowne Street
Cambridge, MA 02139
Telephone - 617-444-3227
Facsimile - 617-551-8820